



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁴ : A61K 39/12, 39/17, 39/215 A61K 39/255, 39/39	A1	(11) International Publication Number: WO 86/ 00811 (43) International Publication Date: 13 February 1986 (13.02.86)
(21) International Application Number: PCT/HU85/00048 (22) International Filing Date: 29 July 1985 (29.07.85) (31) Priority Application Number: 2919/84 (32) Priority Date: 30 July 1984 (30.07.84) (33) Priority Country: HU (71)(72) Applicant and Inventor: CSATÁRY, László [HU/HU]; Deres u. 7, H-1124 Budapest (HU). (74) Agent: PATENTBUREAU DANUBIA; Bajcsy-Zsilinszky ut 16, H-1368 Budapest (HU). (81) Designated States: AT (European patent), AU, BE (European patent), BR, CH (European patent), DE (European patent), DK, FI, FR (European patent), GB (European patent), IT (European patent), JP, LU (European patent), MC, NL (European patent), NO, RO, SE (European patent), SU, US.		Published <i>With international search report.</i>
(54) Title: THERAPEUTIC PREPARATIONS FOR TREATMENT OF CERTAIN VIRAL AND OTHER DISEASES AND THE PREPARATION OF THE SAME (57) Abstract Therapeutic preparations against certain viral and other diseases of humans. The preparations are specified as formulas containing attenuated Newcastle disease virus, Marek's disease virus, avian bronchitis virus or avian encephalitis virus, mixed in carrier substance generally used in human pharmacology, if desired along with one or more optional potentiating preparations. Another object of the invention is the use of the above viruses in the treatment of virus diseases as well as malignant and benign tumours and collagen diseases.		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	GA	Gabon	MR	Mauritania
AU	Australia	GB	United Kingdom	MW	Malawi
BB	Barbados	HU	Hungary	NL	Netherlands
BE	Belgium	IT	Italy	NO	Norway
BG	Bulgaria	JP	Japan	RO	Romania
BR	Brazil	KP	Democratic People's Republic of Korea	SD	Sudan
CF	Central African Republic	KR	Republic of Korea	SE	Sweden
CG	Congo	LI	Liechtenstein	SN	Senegal
CH	Switzerland	LK	Sri Lanka	SU	Soviet Union
CM	Cameroon	LU	Luxembourg	TD	Chad
DE	Germany, Federal Republic of	MC	Monaco	TG	Togo
DK	Denmark	MG	Madagascar	US	United States of America
FI	Finland	ML	Mali		
FR	France				

THERAPEUTIC PREPARATIONS FOR TREATMENT OF CERTAIN
VIRAL AND OTHER DISEASES AND THE PREPARATION OF
THE SAME

Technical field

5 The present invention relates to a set of therapeutic preparations (further on Preparation(s)) for the treatment of certain viral and other diseases, together with the complete technics of their production, including all materials and methods used.

10 The Preparations are effective against various pathological conditions caused by the Herpes group of viruses, and against certain malignant and benign tumours and collagen diseases as well.

Background art

15 Inactivated or live attenuated viruses have long been used all over the world for the specific prevention of several viral diseases of humans and animals. We have found that certain attenuated viral vaccines, prepared against some viral diseases of animals (Newcastle disease, Marek's
20 disease, avian bronchitis, avian encephalitis) had a distinct therapeutic effect against various human diseases of known viral or unknown etiology.

Disclosure of invention

25 Accordingly the object of the present invention is a set of preparations containing attenuated (or killed) Newcastle disease virus, Marek's disease virus, avian bronchitis virus or avian encephalitis virus, mixed in a carrier which is acceptable for use in humans. The present invention relates also to all materials and methods used
30 in the production of all preparations.

- 2 -

The Preparations have already been used with very good result in the conditions listed below:

1. The Preparation containing attenuated Newcastle disease virus was active against the following conditions:
 - a) Infections caused by viruses of the Herpes group, such as Herpes simplex I and II; Herpes zooster; Cytomegalovirus; infectious mononucleoses (Epstein-Barr virus)
 - b) Aphthostomatitis
 - c) Verruca vulgaris
 - d) Infantile pharyngeal papilloma
 - e) Human adenocarcinomas
 - f) Collagen diseases (e.g. nodous polyarteritis)
 - g) Rheumatic arthritis
2. The Preparation containing attenuated Marek's disease virus acted against the following conditions:
 - a) Various human cancers (mainly adenocarcinomas)
 - b) Infections caused by viruses of the Herpes group as listed above (1.a)
3. The Preparation containing attenuated avian bronchitis virus was active against the following conditions:
 - a) Various human cancers
 - b) Infections caused by the above listed (1.a) viruses of the Herpes group.
4. The Preparation containing attenuated avian encephalitis virus was active against the following conditions:
 - a) Various human cancers

While most vaccines used for specific disease prevention in humans contain killed (inactivated) virus, all Preparations contain live attenuated virus. The possible mechanism of action of the Preparations is thus either an interference with the

- 3 -

virulent viruses responsible for the actual disease, or a highly efficient aspecific stimulation of the natural protective mechanisms operative in the organism involved by disease.

5 The Preparations are produced by suspending live attenuated or inactivated, purified or highly purified and concentrated viruses in one of the carrier substances generally used in human pharmacology. The Preparations may be supplemented with potentiating drugs (e.g. tranquilizers).

10 The optimal form of delivery of the Preparations is in a freeze-dried form, in sealed ampoules, with the diluent supplied in a separate vial. In this form, the Preparations can be stored at room temperature for a practically unlimited time. Another forms of delivery are in solution, suppository, capsule, emulsion, suspension, ointment, etc. These should
15 be stored in cold, for their activity may decay rapidly at room temperature.

The dosage of the Preparations depends of their actual composition and form, on the patient's general condition, and on stage (severity) of the disease actually treated.

20 The Preparations are non-toxic, and have no side effect whatever.

The Preparations were tested in humans and animals, and showed a great therapeutic efficiency in both clinical and experimental trials.

- 4 -

Claims

1. Therapeutic preparation for the treatment of viral diseases and against malignant and benign tumours and collagen diseases characterized by containing live attenuated viruses selected from the group consisting of Newcastle disease virus, Marek's disease virus, avian bronchitis virus and avian encephalitis virus.
2. The preparation according to claim 1 characterized by containing at least one carrier.
3. Use of Newcastle disease virus, Marek's disease virus, avian bronchitis virus and avian encephalitis virus in the treatment of viral diseases, against malignant and benign tumours and collagen diseases.
4. The use of viruses according to claim 3 in the treatment of diseases caused by the Herpes group of viruses.

INTERNATIONAL SEARCH REPORT

International Application No PCT/HU 85/00048

I. CLASSIFICATION OF SUBJECT MATTER (If several classification symbols apply, indicate all) *		
According to International Patent Classification (IPC) or to both National Classification and IPC		
IPC ⁴ A 61 K 39/12, 39/17, 39/215, 39/255, 39/39		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System	Classification Symbols	
Int. Cl. ⁴	A 61 K 39/12, 39/17, 39/215, 39/255	
Documentation Searched other than Minimum Documentation to the extent that such documents are included in the fields searched ⁸		
III. DOCUMENTS CONSIDERED TO BE RELEVANT ⁹		
Category ⁹	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
X	Patent Abstracts of Japan, unexamined applications, section C, vol. 7, no. 219, issued 30 March 1983, The Patent Office Japanese Government, page 76 C 188, see Kokai-no. 58-116 422 (Midori Juji K.K.).	(1,2)
X	US, A, 3 548 054 (R.E. BOWEN et al.) -15 December 1970 (15.12.70), see column 2, line 10.- column 3, line 4.	(1,2)
X	GB, A, 1 274 820 (TAKEDA YAKUHHIN KOGYO KABUSHIKI KAISHA) 17 May 1972 (17.05.72), see claims 1,11-13.	(1,2)
X	AT, B, 346 476 (M. SEVOIAN) 10 November 1978 (10.11.78), see claims 1,13.	(1,2)
X	US, A, 3 674 861 (A.E. CHURCHILL) 04 July 1972 (04.07.72), see abstract; claims 12,13; examples 2,5,6; column 1, lines 1-6.	(1,2)
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>* Special categories of cited documents: ¹⁰</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"A" document member of the same patent family</p> </div> </div>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search 11 October 1985 (11.10.85)		Date of Mailing of this International Search Report 16 October 1985 (16.10.85)
International Searching Authority AUSTRIAN PATENT OFFICE		Signature of Authorized Officer <i>Imboden</i>

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category *	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No
A	EP, A1, 0 086 025 (AKZO N.V.) 17 August 1983 (17.08.83), see claims 1,3.	(1,2)
A	US, A, 4 357 320 (P. APOUTOWEIL, M.M. KRAS-SELT) 02 November 1982 (02.11.82), see abstract; claims 1-7.	(1,2)
A	US, A, 4 049 794 (O.-C. STRAUB) 20 September 1977 (20.09.77), see abstract; column 1, line 65 - column 4, line 49.	(1,2)
A	DE, A, 2 120 929 (MERCK & CO INC.) 18 November 1971 (18.11.71), see claims 1,2.	(1,2)
A	DE, A, 1 492 083 (PHILIPS ROXANE INC.) 07 August 1969 (07.08.69), see page 1, line 1 - page 4, line 16.	(1,2)
A	AT, B, 343 797 (H. STICKL) 12 June 1978 (12.06.78), see claim 1.	(1,2)
A	FR, A, 2 444 467 (GIST-BROCADES N.V.) 18 July 1980 (18.07.80), see claims 1,5,6; page 8, lines 5-24.	(1,2)

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

V. ☐ OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE :

This international search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. ☒ Claim numbers 3, 4 because they relate to subject matter not required to be searched by this Authority, namely:

Methods for treatment of the human or animal body by therapy -
see Article 17(2)a)i) and Rule 39.1, iv).

2. ☐ Claim numbers because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim numbers because they are dependent claims and are not drafted in accordance with the second and third sentences of PCT Rule 6.4(a).

VI. ☐ OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING :

This International Searching Authority found multiple inventions in this international application as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.
2. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:
3. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claim numbers:
4. ☐ As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

- ☐ The additional search fees were accompanied by applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

Anhang zum internationalen Recherchenbericht über die internationale Patentanmeldung Nr.

In diesem Anhang sind die Mitglieder der Patentfamilien der im obengenannten internationalen Recherchenbericht angeführten Patentedokumente angegeben. Diese Angaben dienen nur zur Unterrichtung und erfolgen ohne Gewähr.

Annex to the International Search Report on International Patent Application No. PCT/HU 85/00048

This Annex lists the patent family members relating to the patent documents cited in the above-mentioned International search report. The Austrian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Annexe au rapport de recherche internationale relatif à la demande de brevet international n°.

La présente annexe indique les membres de la famille de brevets relatifs aux documents de brevets cités dans le rapport de recherche internationale visé ci-dessus. Les renseignements fournis sont donnés à titre indicatif et n'engagent pas la responsabilité de l'Office autrichien des brevets.

Im Recherchenbericht angeführtes Patent- dokument Patent document cited in search report Document de brevet cité dans le rapport de recherche	Datum der Veröffentlichung Publication date Date de publication	Mitglied(er) der Patentfamilie Patent family member(s) Membre(s) de la famille de brevets	Datum der Veröffentlichung Publication date Date de publication
JP-A2-58 116 422	30/03/1983	None	
US-A - 3 548 054	15/12/1970	None	
GB-A - 1 274 820	17/05/1972	CA-A1- 962 593	11/02/1975
		DE-A -2 058 645	09/06/1971
		DE-C2-2 058 645	11/02/1982
		DK-B - 124 340	09/10/1972
		ES-A1- 385 968	16/11/1973
		FR-A1-2 073 436	01/10/1971
		FR-A5-2 073 436	01/10/1971
		FR-B1-2 073 436	30/08/1974
		NL-A -7 017 334	02/06/1971
		NL-B - 170 595	01/07/1982
		NL-C - 170 595	01/12/1982
AT-B - 346 476	10/11/1978	AR-A1- 201 878	24/04/1975
		AT-A - 6 002/74	15/03/1978
		AU-A1-70 962/74	08/01/1976
		BE-A1- 817 865	18/11/1974
		DE-A1-2 434 515	27/03/1975
		DK-A - 3 895/74	10/03/1975
		DK-B - 137 931	05/06/1978
		DK-C - 137 931	30/10/1978
		ES-A1- 428 370	16/09/1976
		FI-A - 219 974	20/01/1975
		FR-A1-2 301 268	17/09/1976
		FR-B1-2 301 268	21/07/1978
		GB-A -1 481 847	03/08/1977
		IE-B - 40 159	28/03/1979
		IL-A0- 45 181	22/10/1974
		IT-A -1 017 330	20/07/1977
		JP-A2-50 052 227	09/05/1975
		NL-A -7 409 842	21/01/1975
		NO-A - 742 557	21/01/1975
		SE-A -7 409 411	20/01/1975

Fortsetzung siehe Blatt 2

AT-B - 346 476	10/11/1978	US-A-3 981 771	21/09/1976
		ZA-A- 743 771	30/07/1975
US-A - 3 674 861	04/07/1972	BE-A - 741 865	19/05/1970
		BG-D - 20 617	05/12/1975
		CA-A1- 966 779	29/04/1975
		DE-A - 1 957 747	11/06/1970
		DK-B - 131 545	04/08/1975
		DK-B - 131 609	11/08/1975
		DK-C - 131 545	29/12/1975
		DK-C - 131 609	19/01/1976
		ES-A1- 373 631	16/05/1972
		FR-A5- 2 023 537	20/08/1970
		FR-B1- 2 023 537	08/06/1973
		GB-A - 1 292 803	11/10/1972
		IL-A0- 33 318	29/01/1970
		IL-A1- 33 318	29/06/1973
		IT-A - 1 056 006	30/01/1982
		JP-B4-49 035 144	20/09/1974
		NL-A - 6 917 014	20/05/1970
		RO-P - 61 995	15/06/1977
EP-A1-O 086 025	17/08/1983	AU-A1- 10 769/83	11/08/1983
		CA-A1- 1 189 450	25/06/1985
		DK-A0- 470/83	31/01/1983
		DK-A - 470/83	06/08/1983
		ES-A1- 519 551	16/03/1984
		ES-A5- 519 551	13/04/1984
		GB-A1- 2 114 438	24/08/1983
		IL-A0- 67 820	15/06/1983
		JP-A2-58 146 513	01/09/1983
		ZA-A - 830 430	26/10/1983
US-A -4 357 320	02/11/1982	US-E - 31 830	12/02/1985
		US-A - 4 500 638	19/02/1985
		US-A - 4 505 892	19/03/1985
		AR-A1- 222 263	30/04/1981
		AT-E - 4 510	15/09/1983
		CA-A2- 1 183 473	05/03/1985
		CA-A1- 1 184 115	19/03/1985
		CA-A2- 1 184 116	19/03/1985
		DK-A - 5 052/80	31/05/1981
		EP-A2- 0 030 063	10/06/1981
		EP-A3- 0 030 063	14/04/1982
		EP-B1- 0 030 063	24/08/1983
		ES-A1- 497 255	01/11/1981
		ES-A5- 497 255	24/11/1981
		JP-A2-56 092 823	27/07/1981
		NL-A - 7 908 687	01/07/1981
		PT-A - 72 077	01/11/1980
		PT-B - 72 077	29/09/1981
		ZA-A - 807 459	25/11/1981
		NL-A - 8 005 083	01/04/1982
		NL-A - 8 005 063	01/04/1982

US-A-4 049 794 20/09/1977

US-A -	4	017 359	12/04/1977
US-A -	4	039 656	02/08/1977
AT-A -	10	419/72	15/03/1975
AT-B -		326 817	29/12/1975
AU-A1-	49	920/72	13/06/1974
BE-A1-		792 484	08/06/1973
BG-D -		21 417	20/05/1976
CA-A1-		988 848	11/05/1976
CH-A -		577 558	15/07/1976
CS-P -		189 587	30/04/1979
DD-C -		108 115	12/09/1974
DE-A1-	2	161 344	20/06/1973
DE-B2-	2	161 344	08/05/1980
DK-B -		143 201	20/07/1981
DK-C -		143 201	14/12/1981
ES-A1-		409 464	16/03/1976
FR-A1-	2	162 637	20/07/1973
FR-B1-	2	162 637	02/07/1976
GB-A -	1	356 076	12/06/1974
HU-P -		167 086	28/08/1975
IE-B -		36 995	13/04/1977
JP-A2-	48	062 912	01/09/1973
JP-A2-	48	062 919	01/09/1973
JP-B4-	59	024 137	07/06/1984
JP-B4-	60	011 013	22/03/1985
NL-A -	7	216 628	13/06/1973
NL-B -		178 014	01/08/1985
PH-A -		12 597	27/06/1979
SE-A -	8	400 283	20/01/1984
SE-A0-	8	400 283	20/01/1984
SU-D -		439 956	15/08/1974
ZA-A -		728 709	29/08/1973

DE-A-2 120 929 18/11/1971

AT-B -		317 421	26/08/1974
AT-B -		317 606	10/09/1974
BE-A1-		766 492	16/09/1971
BR-A0-	7	102 066	13/03/1973
CA-A1-		934 295	25/09/1973
CH-A -		565 863	29/08/1975
CS-P -		191 868	31/07/1979
DE-B2-	2	120 929	28/06/1979
DK-B -		133 311	26/04/1976
DK-C -		133 311	20/09/1976
ES-A1-		390 698	01/07/1973
FR-A5-	2	092 112	21/01/1972
FR-B1-	2	092 112	06/09/1974
GB-A -	1	316 168	09/05/1973
GB-A -	1	317 710	23/05/1973
HU-P -		162 835	28/04/1973
IE-B -		35 138	26/11/1975
IE-B -		35 139	26/11/1975
IL-A0-		36 329	26/05/1971

Fortsetzung siehe Blatt 4

DE-A-2 120 929	18/11/1971	IL-A1- 36 329	25/04/1975
		IT-A - 1 045 525	10/05/1980
		JP-B4-48 041 534	07/12/1973
		NL-A - 7 100 529	02/11/1971
		NL-B - 165 217	15/10/1980
		NL-C - 165 217	16/03/1981
		PL-P - 76 295	28/02/1975
		US-A - 3 642 574	15/02/1972
		YU-A - 625/71	31/10/1980
		YU-B - 35 785	30/06/1981
		ZA-A - 711 382	29/11/1972
		BR-AO- 7 401 519	31/12/1974
DE-A-1 492 083	07/08/1969	DK-B - 116 232	22/12/1969
AT-B- 343 797	12/06/1978	AT-A - 5 989/75	15/10/1977
		BE-A1- 831 691	17/11/1975
		CA-A1- 1 057 195	26/06/1979
		CH-A - 614 627	14/12/1979
		DE-A1- 2 437 166	19/02/1976
		DE-B2- 2 437 166	27/01/1977
		DE-C3- 2 437 166	13/10/1977
		DK-A - 3 477/75	02/02/1976
		DK-B - 141 835	30/06/1980
		DK-C - 141 835	10/11/1980
		ES-A1- 439 966	01/03/1977
		FR-A1- 2 280 390	27/02/1976
		FR-B1- 2 280 390	11/04/1980
		GB-A - 1 517 540	12/07/1978
		JP-A2-51 041 420	07/04/1976
		NL-A - 7 509 136	03/02/1976
		SE-A - 7 508 565	02/02/1976
		US-A - 4 053 582	11/10/1977
		ZA-A - 754 725	30/06/1976
FR-A-2 444 467	18/07/1980	AT-E - 6 125	15/02/1984
		BE-A1- 880 777	20/06/1980
		CA-A1- 1 136 043	23/11/1982
		DK-A - 5 472/79	21/06/1980
		EP-A1- 0 013 449	23/07/1980
		EP-B1- 0 013 449	08/02/1984
		ES-A1- 487 062	16/12/1980
		ES-A5- 487 062	16/01/1981
		ES-A1- 494 598	16/05/1981
		ES-A5- 494 598	16/06/1981
		FR-A1- 2 444 467	18/07/1980
		FR-B1- 2 444 467	02/11/1984
		JP-A2-55 089 232	05/07/1980
		LU-A - 82 018	23/07/1981
		NL-A - 7 812 359	24/06/1980
		PT-A - 70 556	01/12/1979
		US-A - 4 515 777	07/05/1985
		ZA-A - 796 944	26/11/1980
		NL-A - 7 903 299	28/10/1980